REMARKS

Support for new Claim 43 can be found throughout the specification, e.g., Page 1, 2nd paragraph, line 2; Example 1, particularly, e.g., Page 7.

Rejection under §112, second paragraph

The term "human-compatible" in Claim 1 has been replaced with the term "humanized." Support for this amendment can be found in the specification, e.g., Paragraph spanning Pages 2-3; Page 3, 2nd paragraph, line 5.

Rejections under §102 and §103

On Page 5 of the Office action, it is stated that "given, that the prior art agonistic CD28-specific antibodies stimulated T cells via a primary activation signal or the CD3 complex such as anti-CD3 antibody (e.g. see column 5, paragraphs 1-3), the prior art CD28-specific antibodies stimulated T cells directly without occupancy of antigen receptor of human T lymphocytes (e.g., T cell receptor)."

However, the experiments performed in U.S. Pat. No. 5,858,358 to June et al. (hereinafter, "the '358 Patent") were accomplished using anti-CD3 antibody which stimulates the T-cell receptor by binding to the T-cell TCR/CD3 complex. See, e.g., '358 Patent, Column 4, lines 45-47. CD3 is a part of the TCR complex. See, Specification, Page 7, 5th paragraph, lines 1-2. The present specification indicates that occupancy of the T-cell antigen receptor ("TCR") includes binding by an antibody (such as an anti-CD3 antibody). See, Specification, Page 1, 2nd paragraph, lines 9-11; Page 7, 5th paragraph. Receptor occupancy is excluded by the claim 1 ("without occupancy of an antigen receptor"). Consequently, the '358 does not disclose the claimed invention.

The '358 patent mentions, but does not enable, "directly stimulating receptor-coupled signaling pathways." '358, Column 2, lines 19-20. In order for a disclosure to anticipate a claim, it must be enabling. See, e.g., *Constant v. Advanced Micro-Devices*, 848 F.2d 1560; 7 USPQ2d 1057 (Fed. Cir. 1988). Moreover, the direct stimulation is delivered in combination with an anti-CD28 antibody. Thus, both receptor stimulation and CD28 binding were utilized to cause cell proliferation. See, e.g., '358 Patent, Column 2, lines 23-30. This disclosure therefore does not anticipate an antibody which,

e.g., causes T-cell proliferation upon binding to said CD28 on all classes of said T-cells without T-cell receptor stimulation. See, e.g., Claim 43.

Finally, the '358 patent also does not disclose humanized antibodies.

Taken together, it is evident that '358 Patent does not anticipate the claimed invention.

The '358 Patent in combination with Tacke et al. do not render the claimed invention obvious, as alleged on Page 6 of the Office action. As spelled out clearly in the response filed by applicant on April 28, 2003, the antibodies disclosed in the '358 Patent do not cause T-cell proliferation upon binding to said CD28 on all classes of said T-cells, and, e.g., without T-cell receptor stimulation. Compare, e.g., Claim 1 and 43. The disclosure in Tacke et al. do not remedy this deficiency. Even if Tacke et al could have provided a reasonable expectation of success as alleged in the Office action (which applicants do not admit that it does), it is shattered by the facts about the '358 Patent's human anti-CD28 antibodies discussed in the April 28, 2003 response. These antibodies do not possess all the claimed properties (e.g., causing T-cell proliferation upon binding to said CD28 on all classes of said T-cells, and, e.g., without T-cell receptor stimulation). Given these facts, the skilled worker would not have had a reasonable expectation of success that a human anti-CD28 could be generated having the claimed properties. The '358 patent clearly teaches away from it.

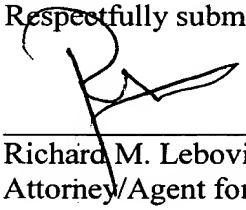
It is not understood why the rejection over Siefken et al. has been maintained. As already argued, Siefken et al. disclose the BW 828 required crosslinking to induce proliferation, and therefore was not without said antibody being artificially crosslinked with a secondary antibody. See, e.g., Siefken et al., Page 61, Table 2.

In view of these comments, withdrawal of the rejections is respectfully requested.

In view of the above remarks and amendments, favorable consideration is courteously requested. However, if there are any remaining issues which can be expeditiously resolved by a telephone conference, the Examiner is courteously requested to telephone the undersigned at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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